REMARKS

Claims 1, 4-8, 10, 11, 13, 14, 17-21, 23, 24, 27-30, and 32-34 are currently pending. Claims 10, 13, 17, and 34 have been canceled. Claims 1, 4, 5, 8, 14, 18, 19, 24, 27, and 28 are currently amended. Claim 32 is withdrawn. Claims 35-37 are new. Support for the claim amendments and new claims may be found throughout the specification and claims as originally filed, including, for example, in the specification as published (U.S. Publication No. 2004/0259101) in paragraphs 0005-0006 (claim 1); paragraph 0010 (claims 1, 14, and 24); paragraph 0013 (claims 5, 18, and 27); paragraph 0024 (claim 1); paragraphs 0031 and 0033 (claims 1, 14, and 24); paragraphs 0044-0051 (claims 1, 14, and 24); paragraphs 0058-0061 (claims 1, 14, 24, and 35-37); and paragraphs 0068 and 0070-0071 (claims 14 and 24). Applicant believes that no new matter is presented by the amendment.

Amendment of the originally filed claims, or cancellation of any claims should in no way be construed as an acquiescence, narrowing, or surrender of any subject matter. The amendments are being made not only to point out with particularity and to claim the present invention, but also to expedite prosecution of the present application.

Rejections under 35 U.S.C. § 112, Second Paragraph

The Office rejected claims 1, 4-8, 11, 14, and 17-21 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for omitting essential steps.

Applicant respectfully disagrees, but, without acquiescing to the Office's position, has amended claim 1 to recite, in part, "a method for identifying a patient as a candidate for additional colorectal cancer testing". Applicant has also amended the "determining" step as indicated in the listing of claims. Support for these amendments are found throughout the specification, for example, in paragraphs 0005-0006 of the published application. Each of claims 4-8 and 11 depends directly or indirectly from claim 1. No new matter has been added.

Further, without acquiescing to the Office's position, Applicant has amended claim 14 to recite a step of "performing at least one additional assay on a stool sample from the patient identified as a positive screen, wherein a positive result of said at least one additional assay indicates the patient has abnormal proliferating colorectal cancer cells". Support for this

amendment is found throughout the specification, for example, in paragraphs 0058-0061, 0068, and 0070-0071 of the published application. Each of claims 18-21 depends directly or indirectly from claim 14. Claim 17 has been canceled rendering the rejection of this claim moot. No new matter has been added.

Accordingly, Applicant respectfully requests withdrawal of these rejections.

Rejections under 35 U.S.C. § 112, First Paragraph

The Office rejected claims 24, 27-30, and 33 under 35 U.S.C. § 112, first paragraph alleging failure to comply with the enablement requirement. Without acquiescing to the Office's position, Applicant has amended claim 24 to recite "colorectal cancer." Each of claims 27-30 and 33 depends directly or indirectly from claim 24. No new matter has been added.

Accordingly, Applicant respectfully requests withdrawal of this rejection.

Rejections under 35 U.S.C. § 103

The Office rejected claims 1, 4, 7, 11, 14, 17, 20, 24, 29, and 33 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Loktionov *et al.* (Clinical Research, 1998, 4:337-342) in view of Hromadnikova *et al.* (BMC Pregnancy and Childbirth, 2002, 2:1-5). Applicant respectfully traverses the rejection.

The Office, on page 9 of the instant action, asserts, "Loktionov *et al.* teaches a method of diagnosing and screening a patient for the presence of colorectal cancer comprising measuring quantitative amounts of patient genomic DNA in a stool sample comprising shed cells or shed debris wherein the quantitative amounts are measured by measuring amounts of fragments of less than 200 bp."

Loktionov *et al.*, however, does not disclose measuring genomic DNA from a stool sample comprising shed cells and cellular debris, where such DNA may be substantially degraded. Rather, the method disclosed in Loktionov *et al.* teaches measuring an amount of DNA extracted from whole cells. Specifically, Loktionov *et al.* teaches isolating exfoliated colonocytes using magnetic beads coated with epithelium-specific antibodies and washing the whole cells before DNA extraction and quantitation. Loktionov *et al.* does not disclose or suggest isolating DNA from cellular debris. DNA obtained from exfoliated normal cells (i.e.,

noncancerous cells) is different than DNA obtained from exfoliated cancer or precancer cells because normal exfoliated cells typically have undergone apoptosis, and thus, produce cellular debris comprising DNA that has been substantially degraded. Therefore, the method of Loktionov *et al.* cannot determine a quantitative amount of all genomic DNA that is present in a stool sample because it isolates whole cells prior to DNA extraction and quantitation.

In addition, Loktionov *et al.* does not teach or disclose determining genome equivalents of patient genomic DNA by measuring an amount of nucleic acid fragments, said fragments having length of 200 bp or less. Loktionov *et al.* teaches determining an amount of nucleic acid by measuring an absorbance measurement at 260 and 280 nm. Such an absorbance measurement cannot discriminate DNA fragments based on size, and is unreliable if contaminating material is present in the sample. While Loktionov *et al.* describes the amplification of a 113-bp fragment of K-ras, it performs this PCR reaction only to confirm DNA quality of the extracted DNA, not to determine the amount of DNA in the sample. Thus, there is no suggestion in Loktionov *et al.* that a total complement of genomic DNA as determined by measuring an amount of nucleic acid fragments having length of 200 bp or less could distinguish normal subjects from cancer patients. Therefore, there is no reasonable expectation of success based on the cited prior art that determining genome equivalents of patient genomic DNA by measuring an amount of nucleic acid fragments having length of 200 bp or less could be used as a screen to positively identify a patient as having cancer.

The Office, in page 10 of the instant action, states that while "Loktionov *et al.* does not specifically teach that the genomic DNA amounts are measured in terms of 'genome equivalents'[,] these deficiencies are made up in the teachings of Hromadnikova *et al.*" Applicant respectfully traverses the rejection. Hromadnikova *et al.*, does not cure the deficiencies of Loktionov *et al.* because neither reference teaches nor suggests determining a quantitative amount of genome equivalents by measuring an amount of fragments, said fragments having length of 200 bp or less.

Accordingly, withdrawal of this rejection is respectfully requested.

The Office rejected claims 1, 4-8, 11, 14, 17-21, 24, 27-30, and 33 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Loktionov *et al.* (Clinical Research, 1998, 4:337-

342) in view of Hromadnikova *et al.* (BMC Pregnancy and Childbirth, 2002, 2:1-5) and further in view of Ahlquist *et al.* (Gastroenterology, 2000, 119:1219-1227).

The Office, on page 11 of the instant action states:

> The combined teachings of Loktionov *et al.* and Hromadnikova et al. do not specifically teach methods of detecting the presence of abnormal proliferating colorectal cancer cells/detecting colorectal cancer/diagnosing colorectal cancer by: (1) performing a DNA integrity assay; (2) detecting a ras mutation, or (3) performing a colonoscopy. However, these deficiencies are rendered obvious or made up in the teachings of Ahlquist *et al.*

Applicant respectfully traverses the rejection. None of Loktionov *et al.*, Ahlquist *et al.*, or Hromadnikova *et al.* teaches or suggests determining a quantitative amount of genome equivalents by measuring an amount of fragments, said fragments having length of 200 bp or less.

Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicant respectfully requests reconsideration of the rejections and Applicant request allowance of pending claims 1, 4-8, 11, 14, 18-21, 24, 27-30, and 32-33 in due course. The Examiner is cordially invited to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance, or if there are any questions regarding this case.

Respectfully submitted,

Date: February 22, 2008
Reg. No. 57,961

/Charlene A. Stern-Dombal/
Charlene A. Stern-Dombal
Agent for Applicant
Goodwin Procter LLP
Exchange Place
Boston, Massachusetts 02109
Goodwin Customer No. 051414

Tel. No.: (617) 570-8382
Fax No.: (617) 523-1231

LIBC/3217770.1